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E D I T O R I A L

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful—the editor, alone, is responsible for their type, their tone and their tenor.

NOISE!

THE noise of molecules may not be heard by the human ear unaided, thanks to our fortunate aural design. And the noiseless foot of time is another kindred kindness.

But there are noises that are as much of a nuisance and an annoyance as they are unnecessary. These are the pathologic noises—booming, clanging, whistling, trumpeting, screeching, buzzing noises that sear our sensitive souls and send our senses helter-skelter to a sound-proof shelter.

They do more injury to our delicate nervous tendrils than do unpleasant scenes or putrescent smells, and the countryward trek of so great a number of our erstwhile urban dwellers is simply a search after peace and a surcease from the raucous, strident, stentorian babble of the city's bubbling business.

From a little house organ† published in the interest of a chemical supply house we print in the foregoing connection this interesting series of informative paragraphs.

In the last few years there has been a great noise made about noise. This is not as modern as it seems, for the cultured Greeks of Sybaris in 700 B. C. had regulations against noise.

Schopenhauer, the German philosopher said, "noise is a true murderer of thought." Herbert Spencer, the great scientist is quoted, "you might gauge a man's intellectual capacity by the degree of his intolerance of unnecessary noise."

This is the "Age of Noise" and certainly we are becoming more and more conscious that the evil of noise is an "impurity" to be measured and dealt with as chemical impurities—eliminated.

When noise measuring devices are gathered together in one place, for the purpose of testing noise, we have a new and unique analytical room, a noise laboratory.

† The Laboratory.

These laboratories are growing in numbers. Some are motor buses fully equipped to measure street noises, others are located in manufacturing plants, to test the noise of fans, motors, ventilators, vacuum cleaners, refrigerators and numerous appliances of our modern age.

Noise cannot be weighed or titrated and the results expressed in grams or cubic centimeters, but it can be measured electrically and expressed in units of loudness, called decibels.

This unit, the decibel, has been defined as the smallest increment which the average human ear can detect. For those who are more exacting, a decibel is a ratio of intensities. If the electrically measured intensities of two sounds are in a ratio of 10 to 1 they differ by 10 decibels. The difference between loudness in the average ear, as measured approximately by decibels, and sound energy as measured by electrical instruments, is apparent from the following comparison:

Decibels	Intensity as measured electrically
10.....	10
20.....	100
30.....	1000
40.....	10,000
50.....	100,000
100.....	10,000,000,000

The scientific instrument necessary to a modern noise laboratory is the noise meter, or acoustimeter, used to measure decibels.

This instrument is portable, and can be read as easily as a thermometer or voltmeter. Its range is 30 to 120 decibels. A noise of 30 decibels is about that of the average country residence. One of 120 decibels is above that of an airplane engine five feet from the ear.

The acoustimeter consists of a precision microphone, radio amplifiers and an electrical meter for indicating the intensity of sound entering the microphone. Accessories such as frequency selectors, oscillographs and oscilloscopes can be added to give a more complete analysis.

There has been recently developed a special pick-up device, or selective microphone, which is capable of responding to the noise from a local area such as a piano wire or one part of a machine.

When the vacuum cleaner or electric refrigerator salesman calls and says his product is more silent than his rival's, it might be interesting to know in decibels, how much quieter.

Authors are partial to the simile "as loud as a lion's roar." Here is the measure of a lion's roar compared to the roar of tigers.

A lion's roar = 87 decibels.

A Siberian tiger's roar = 79.5 decibels.

A Bengal tiger's roar = 75.5 decibels.

The noise meter now enables the prosecution of offenders in courts of law, and thus makes it possible to administer many old and heretofore impracticable ordinances.

All, except the deaf, are conscious of noises but it requires acoustimeter measurements to bring about a realization of their relative intensities.

Five subway turnstiles produced a noise of 83 decibels which is 7.5 decibels greater than the Bengal tiger's roar. Practically all of that noise is avoidable.

Restrictions were put upon the loud speakers of "Radio Row" when measurements showed that at their best, or worst, they were doing 79 decibels.

A recent anti-noise ordinance in Minneapolis requires milkmen to use rubber lined bottle racks, to wear rubber heels and to shoe their horses with rubber horseshoes.

More power, we say, to decibels if they toll for the end of needless noise, and so bring poise and peace to all of us.

A Satisfactory Method of Generating Hydrogen Sulfide.

V. T. Jackson and F. C. Suhrer. *Jour. Chem. Ed.*, 15, 179 (1938). It has been known for some time that a mixture of paraffin and sulfur, available commercially under the name "aichttues," evolves hydrogen sulfide when heated. The authors have found that if a mixture of equal parts of rosin and sulfur is prepared and heated in a test-tube, hydrogen sulfide is easily evolved. It is not necessary to grind the substances finer than to pass through a 20-mesh sieve. If one gram of each of the substances is used, the quantity of gas liberated is sufficient for an ordinary analytical precipitation. The carbon is rather friable and easily removed.

A. O.

SELECTED EDITORIAL

THE PHARMACEUTICAL FARMER*

THE Drug Store still sells drugs. Herbs, under the technical name "botanicals," are used and doubtless will remain in use for years as source materials for medicinal, insecticidal and odoriferous chemical substances. The present vogue for pure concentrates calls not only for synthetic materials from the chemical factories, but also for the essential ingredients of many natural products, under the name "isolates." While Dalmatian Insect Powder is still in demand, there is developing a strong preference for its pyrethrins in the form of concentrated extract. In similar vein, extracts of the drug Ephedra yield the pure active ingredient ephedrine,† used in remedies for hay fever, asthma and certain types of stuffy heads.

Drugs are plants, and as such are objects for agricultural consideration. There has always been interest in drug plants in America. Sassafras plants brought back by Columbus amazed the doctors of Spain by possession of strong and different tastes in leaf, bark and root, suggesting new and powerful curative agents, and made certain that a country with such medicinal resources could not long remain untapped. The first herbs of interest were mostly those used by the Indians for medicine. Then came the finding that Ginseng was of enormous interest to the Chinese, because of its curious bifurcated root, which suggested curative value for all body ailments. A large and profitable business has continued for us in this herb, which, curiously enough, the Chinese have been unable to raise successfully in their own country.

Later, attempts were made to raise Peppermint and Spearmint commercially. This has worked out well, and we now raise a large percentage of our own needs, and even export oils of these plants. Mint, like hay, is harvested by machinery, and the labor cost for producing the active ingredient, the oil, is relatively low. Some other drugs, such as Digitalis, have been raised in the past, showing that they can be grown here, but they cannot be raised with profit at present, with hand-labor prices.

* From the Industrial Bulletin of Arthur D. Little, Inc.

† Now synthetically prepared.

Pyrethrum, related to the spring-blooming perennial pink daisy of our home gardens, is imported in very large quantities, originally from Dalmatia and now principally from Japan, for the making of fly-sprays. We import only the dried flower heads, which are richest in the active pyrethrins, the numbing agents that "drop" the flies. Pyrethrum has been found to grow well in this country, in Pennsylvania, Maryland, Connecticut, Massachusetts, the Great Lakes States and parts of Nebraska and South Dakota. The development of suitable agricultural machinery may make commercial the raising of this large crop. If the plant is raised in this country, it may be economical to extract the pyrethrins from other parts of the plant as well as from the flower heads. With this particular perennial, a crop cannot be obtained before the second year, and large yields probably not before the third.

According to Department of Commerce reports, our exports of crude drugs for the first eight months of 1936 were about \$419,000, and our imports for the same period, \$4,314,000. It seems reasonable that a considerable part of this discrepancy may be corrected by the development of adequate planting, weeding, cultivating and harvesting machinery, as well as by the use of the best plant-management methods now being worked out by the Government and by various institutions.

The better crude-drug houses are quite willing to cooperate to produce American supplies where this is feasible. A Boston drug house, for instance, has advised New Hampshire authorities that it would gladly purchase its annual requirements of 20,000 pounds of dried *Digitalis* if the Granite State can produce an herb of the required quality. This and similar offers cheer New Hampshire farmers to recover a former million-dollar-a-year local agricultural industry.

Each kind of plant has its individuality of requirements of soil, climate and culture, and it is not to be expected that a given grower can handle all types of plants in one locality. At the present time, it appears that desert country in Arizona, California, and New Mexico, as well as in South Dakota, looks best for the raising of *Ephedra*. Peppermint and other mints, Pinkroot and *Angelica* grow best in rich moist soils. Lavender and Larkspur thrive best in well-drained sandy soils, particularly in limestone areas. Ginseng, Goldenseal and

Canada Snakeroot grow best in rich soil in partial shade of forest trees.

Consistent with the present trend toward agricultural products as sources of raw materials for industry, let us not neglect the medicinal, insecticidal and flavor-making herbs.

The Influence of Hydrogen-Ion Concentration on the Surface Tension of Some Colloidal Solutions. P. W. Perryman and C. F. Selous. *J. Physiol.* 92, 151 (1938). A number of lyophilic systems were examined and the variation of surface tension with hydrogen-ion concentration found. Each system (ovalbumin, serum albumin, serum globulin, gelatin, ovarian cyst fluid, brilliant green) with the exception of casein, shows a minimum value of surface tension at the isoelectric point: all the systems, however, show a maximum rate of surface adsorption at this pH. The exceptional behavior of casein may well be due to impurity and partial denaturation.

It is shown that this surface tension pH relationship may be used for the determination of the isoelectric points of certain lyophilic colloids, and was used to identify the major proteins present in the fluid from an ovarian cyst.

I. C.

ORIGINAL ARTICLE

A METHOD FOR DETERMINING THE ACTION OF CERTAIN ORGANISMS ON NITROGEN DISTRIBUTION IN MILK

G. H. McFadden* and H. H. Weiser**

IT HAS long been known that milk is an excellent medium for the growth and multiplication of many kinds of bacteria. In order that the organisms may be able to use certain milk constituents, such as proteins, the bacteria must split these proteins to simpler forms. The manner in which the various proteins are broken down is not well understood, although it is pretty definitely established certain enzymes secreted by the bacterial cell play a very important part in the breakdown of the protein molecule. Undoubtedly the course of decomposition of the proteins goes through a series of stages: proteoses, peptones, polypeptides, peptides, and amino acids. Many bacteria possess enzymes which act on the amino acids and produce ammonia or amines, carbon dioxide, water and sulfur or phosphorus compounds, depending upon the type of amino acid present.

Since amino acids are probably the chief end products of proteolysis of milk proteins brought about by bacterial activity, a measure of the relative amounts of these compounds formed during the course of proteolysis would be valuable.

The object of the work reported in this paper was to improve or modify a method for determining the amino acid content in milk brought about by bacterial activity, in order that more consistent results might be obtained in following the course of the protein digestion of milk.

Experimental

Strains of the genus *Lactobacillus* that actively coagulate milk were used in this study. The sources of the organisms were as follows: five cultures of *Lactobacillus acidophilus* were obtained from various research laboratories. Ten strains of lactobacilli were isolated

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from dairy products, five being from raw milk, one from pasteurized milk, three from Cheddar cheese, and one from Swiss cheese.

In devising a quantitative method for determining the forms of nitrogen in milk resulting from bacterial action, the method used by Hiller and Van Slyke(1) in their study of protein precipitants was modified to conform with conditions encountered under these circumstances. Briefly, the modified method of nitrogen determinations, using skim milk, consisted of the following steps:

1. Protein material precipitated and removed.
2. Total soluble nonprotein nitrogen determined.
3. Amino acid content determined.
4. Material hydrolyzed and the amino acid content again determined.

Procedure

Three hundred grams of skim milk were sterilized, cooled to 35° C., and inoculated with 1 cc. of an actively growing milk culture. The digestion was allowed to take place for the desired length of time in the incubator at 37° C. The digested milk was removed to an 800 cc. beaker and 200 cc. of 2.5 per cent. trichloroacetic acid added to precipitate the proteins. The digested milk was thoroughly stirred to break up all lumps of material, heated to 40° C., rapidly filtered through a fluted filter, and the residue of protein matter thoroughly washed with distilled water and finally discarded. The filtrate containing the soluble nitrogenous material was retained. It was made alkaline to litmus paper with 50 per cent. sodium hydroxide solution, then faintly acid to litmus paper with dilute acetic acid, after which it was rapidly filtered through a fluted filter, and the residue thoroughly washed with distilled water and discarded. The filtrate and washings were then placed in a two liter round-bottom flask and subjected to a reduced pressure distillation (about 35 mm. of mercury) to remove the excess water. The temperature during the distillation was not allowed to exceed 45° C. After the total volume was reduced to about 50 cc., it was filtered into a 100 cc. volumetric flask. The distilling flask was rinsed with distilled water and the filter washed, first with this solution, then with distilled water. The volume was adjusted to exactly 100 cc. at 20° C. with distilled water. This volume contained the soluble nitrogenous material from the original 300 grams of milk.

Five cc. of the soluble nitrogenous material was analyzed by the Kjeldahl(2) method for total nitrogen.

Ten cc. of the soluble nitrogenous material was analyzed for amino nitrogen by the Van Slyke(3) nitrous acid method using the macro apparatus(4).

Twenty-five cc. of the soluble nitrogenous material was placed in a 120 cc. narrow mouth bottle and 25 cc. of concentrated hydrochloric acid added. The mixture was placed in an autoclave and heated at 100° C. for twenty-four hours. The resulting mixture was poured into a 400 cc. beaker, immersed in an ice bath, after which it was cautiously neutralized with a 70 per cent. sodium hydroxide solution. The temperature was not allowed to exceed 40° C. at any time. The solution was made faintly acid with dilute acetic acid and filtered into a 100 cc. volumetric flask, the container rinsed and the residue washed with distilled water. The volume was adjusted to exactly 100 cc. at 20° C. Ten cc. of this sample was analyzed for amino nitrogen by the Van Slyke(3) nitrous acid method.

Discussion of Method

Trichloroacetic acid(5) was chosen as the protein precipitant for several reasons. It is a reagent that leaves a maximum of soluble nitrogenous material(1) which is desirable for this work. It is cheap and is also easily decomposed into chloroform and carbon dioxide, and may therefore be eliminated from the nitrogenous material by heating. Two hundred cc. of 2.5 per cent. acid added to 300 cc. of the digested milk, after heating for thirty minutes, gave a product which filtered rapidly and produced a clear filtrate.

The amino acid content of the filtrate was determined by the Van Slyke(3) nitrous acid method, using the macro apparatus(4). Total nitrogen was determined by the Kjeldahl method as adopted by the Association of Official Agricultural Chemists(2).

The filtrate containing the soluble nitrogenous material was reduced to a small volume and this volume restored to 100 cc. which gave an ample amount of material for all determinations. It was necessary in reducing the volume to distill under reduced pressure for two reasons: first, it lessened the chance of a breakdown of the nitrogenous complex by heat; and second, the material obtained was of such a nature that it did not foam greatly in the amino nitrogen determination. When the filtrate was distilled at a temperature above 50° C.

the liquid became dark and viscous. This was probably due to a breakdown of carbohydrates. With this type of sample considerable foaming occurred in later determinations. If the temperature and pressure were kept sufficiently low, the resulting sample was less viscous and was a light straw color. Foaming was greatly reduced in the Van Slyke amino nitrogen determination by adding 1 cc. of diphenyl ether(6) to the acetic acid before adding the nitrite solution.

Heating at 100° C. for twenty-four hours in an autoclave gave a more complete hydrolysis of those nitrogenous complexes which might be broken down by the organisms in a sufficient length of time. Neutralization of the hydrolyzed material was carried out at a low temperature to prevent loss of sample by spattering and by volatilization, which occurred when a higher temperature was permitted.

The total nitrogen, amino nitrogen, and amino nitrogen after hydrolysis were determined on 15 cultures of lactobacilli which were grown in milk and the milk incubated at 37° C. for 2, 4, 6, and 8-week periods of incubation. Table I summarizes the range of distribution of the nitrogen in the milk as a result of bacterial activity.

TABLE I

NITROGEN DISTRIBUTION IN 300 GRAMS OF MILK AS A RESULT OF BACTERIAL ACTIVITY INCUBATED AT 2, 4, 6, AND 8 WEEK PERIODS

Time of incubation at 37° C.	Total grams of non-protein nitrogen in 300 Gms. of milk	Non-protein amino nitrogen in 300 Gms. of milk			
		Before hydrolysis		After hydrolysis	
		In grams	Per cent. Total N. P. N.	In grams	Per cent. Total N. P. N.
2 weeks	0.1069-0.1456	0.0204-0.0387	19-26	0.0476-0.0696	39-45
4 weeks	0.1053-0.1379	0.0327-0.0399	29-31	0.0337-0.0517	32-38
6 weeks	0.1181-0.1353	0.0370-0.0444	31-34	0.0242-0.0406	20-30
8 weeks	0.1121-0.1384	0.0380-0.0653	33-47	0.0194-0.0292	17-19

From the data presented, a definite progression in nitrogen distribution products appears to have occurred as the incubation time was lengthened. The amount of amino acid produced in eight weeks was double the amount produced in two weeks, while a proportionate increase occurred in four and six weeks. It was evident that a decrease in amino acids due to hydrolysis took place as the amino acid content increased due to bacterial activity.

Conclusions

The method outlined was found to be quite satisfactory for the study of the action of certain bacteria on nitrogen distribution in milk, as occurring after protein cleavage brought about by bacterial action. The amount of protein converted to amino acids by the organisms in a given length of time could be determined. The process of hydrolysis broke down those protein complexes which might eventually be transformed by the organism into amino acids. By determining the nitrogen distribution in a definite quantity of digested milk, it was possible to indicate the results of the nitrogen conversion on a percentage basis.

References

- (1) Hiller, A., and Van Slyke, D. D.: *J. Biol. Chem.* 53, 253-267 (1922).
- (2) "Standard Methods of Milk Analysis" (6th ed.), p. 78, American Public Health Association, New York, 1934.
- (3) Van Slyke, D. D.: *J. Biol. Chem.* 9, 185-205 (1911).
- (4) Van Slyke, D. D.: *Proc. Soc. Exp. Biol. Med.* 9, 112-113 (1912).
- (5) Greenwald, I.: *J. Biol. Chem.* 21, 61-68 (1915).
- (6) Mitchell, H. H., and Eckstein, H. C.: *J. Biol. Chem.* 33, 373-375 (1918).

Wool Fat: Composition of. A. Heiduschka and E. Nier. *J. pr. Chem.*, 1937, v. 149, p. 98-106; abs. in *J. Soc. Dyers Col.*, Nov. 1937, p. 445. Cerotic acid has been isolated from the fatty acid mixture obtained by saponifying wool fat with alcoholic caustic potash. After purification via the ethyl ester and the lithium salt, it had m. p. 78° C. and was identical with the product isolated from beeswax. Lanocric acid separated as a grey insoluble residue when the mixture of fatty acids was dissolved in ether, and, after recrystallization from carbon tetrachloride, had m. p. 102.5° C. Ceryl alcohol, ischolesterol and cholesterol were isolated from the unsaponifiable fraction of wool fat by several crystallizations and precipitations from ethyl and methyl alcohols, but, contrary to the results of former investigators, no carnaubyl alcohol could be detected.

REPRINTED ARTICLE

THE STERILITY OF ALCOHOL*

By Louis Gershenfeld, Ph. M., B. Sc., P. D.

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and Science, Philadelphia, Pa.

FORTY years ago, Minervini (15) and later other workers demonstrated that non-spore-forming organisms could be killed by alcohol. Diluted alcohol was found to be more effective than alcohol of high concentrations, that of 70 per cent. strength being the most efficient. Minervini using the thread method noted that while a 70 per cent. alcohol killed the *Escherichia* (*Bacillus*) *coli* and *Staphylococcus aureus* in 60 minutes, dehydrated or absolute alcohol required at least 12 hours for the former and more than 3 days for the latter organism before destruction was complete. Olitsky and associates (18) and others, however, have reported that the addition of alcohol to body fluids results in the production of dense coagula which protect microorganisms and prevent penetration by the alcohol.

The inefficiency of alcohol as a germicidal agent for spore-forming bacteria has been demonstrated repeatedly. In 1881, Koch (11) showed that neither dilute nor strong alcohol would kill anthrax spores in 110 days. Minervini (15) and Russ (20) confirmed Koch's work. Stokvis (24) revealed that *B. megatherium* remained viable for 2 weeks in alcohol. Heim (9) was able to cultivate *anthrax bacilli* from infected threads which had been immersed in alcohol for 20 years. Dozier (6) found that alcohol possessed no bactericidal effect upon the spores of *Clostridium botulinum*. Nye and Mallory (17) reported the inefficiency of alcohol upon the spores of *Clostridium welchii* in a routine procedure of disinfecting surgical instruments, such technique having resulted in a serious outbreak of infections following operations. Schmidt, (23) in an investigation of catgut, reported that the sterile catgut threads become infected by alcohol when using terminal sterilization. Coulthard and Sykes (3) reported that vegetative forms of bacteria are destroyed in a few minutes by

* Reprinted from the *American Journal of the Medical Sciences*, March, 1938, No. 3, Vol. 195, pp. 358-361.

concentrations over 60 per cent., but ethyl alcohol was impotent against bacterial spores.

In practice today, no reliance is placed upon the use of alcohol (dilute or strong concentrations) as a bactericidal agent for spore-forming organisms. If used at all, it is employed only against the weak resistant organisms and even here considering the technique when it is used (exposures of less than 5 minutes), the alcohol itself in all probability exerts little or no effect as a bactericidal agent.

Alcohol Employed Parenterally

Alcohol in various concentrations has been used externally; internally it has been consumed (by mouth) as an ingredient of various medicinal preparations or of liquors. More recently, however, parenteral therapy with alcohol has been advocated as an aid in the relief of pain and discomfort in a variety of abnormalities. Dogliotti (5) employed subarachnoid injections of absolute alcohol for the relief of peripheral pain in the lower part of the back, the pelvis and legs. Gilcreest and Mullen (8) advocated epidural and transsacral injections of alcohol for the relief of pain. Ruth, (21) Condamin and Arnulf, (2) Davis, (4) Newman, (16) Saltzstein, (22) Baker (1) and many other workers have employed parenteral alcohol therapy with apparent success. More recently, Pozzi and Belleli (19) employed intravenous injections of alcohol (10 cc. of 33 per cent. alcohol in a 45 per cent. solution of dextrose) and they noted an increase in the bactericidal power of the blood. Meynier (14) discusses the intraspinal (intrathecal) injections of alcohol for intractable pain in the pelvis and lower extremities.

Bacteria in Alcohol

Commercial alcohol has been generally accepted as bacteria-free. Only those workers who concern themselves with problems in disinfection and sterilization were familiar with the actual bactericidal properties of alcohol and had knowledge of the bacterial content of commercial alcohol. With the advent of the more frequent use of alcohol as a disinfectant in surgical procedures and its recent use for parenteral administration, several articles appeared in foreign publications concerning the germ content of commercial alcohol. Many devices and methods of sterilizing alcohol have been described. (13) Even in our own country some manufacturers have marketed ster-

ilized absolute alcohol in ampules to be used for parenteral administration. Recently Kuhn and Dombrowsky, (12) Knorr, (10) and also Eschenbrenner (7) reported on the finding of bacteria, in particular spore-formers, in commercial alcohol. My attention was especially directed to the fact that Knorr (10) found more than half of the thirty-eight samples of commercial alcohol (of different concentrations) laden with sporulating organisms. An examination of the American literature did not record findings of the bacterial content of commercial alcohols used in this country.

Experimental

A survey of the literature and personal conversations with many workers who employ injections of alcohol revealed that at least in this country the alcohol used in such injections is rarely redistilled, Berkfeld-filtered or otherwise treated as in sterilization techniques. Not one case of infection has come to the attention of the workers with whom I spoke, even though a total of several thousands of such injections were given by them. The alcohol used generally is the 95 per cent. (by volume) strength or the absolute product (dehydrated alcohol) obtained directly from the regular stock bottle in the drug-store or clinic, and the amount employed in each injection varies from 0.2 to 2 cc., the dose being usually 0.5 to 1 cc.

Accordingly 125 samples of commercial alcohol, consisting of 100 samples of 95 per cent. and 25 samples of absolute (dehydrated) alcohol were obtained. The samples were collected from retail pharmacies; from the drugstores, clinics, pathologic laboratories and operating rooms in large and small hospitals; from the bacteriologic, pathologic, chemical, operative pharmacy and botanical laboratories in teaching institutions; from containers in the offices of medical practitioners; and from stock cans, carboys and drums. The twenty-five absolute alcohol samples, though collected from twenty-three different places, were in all instances present in one-pint cork-stoppered bottles. The 95 per cent. alcohol samples were obtained from all kinds of containers kept under varying conditions. There were small and large bottles, filled and partially filled, cork and glass-stoppered (some were not even stoppered), carboys, barrels and metal drums.

From each of the 125 samples, 1-cc. and 2-cc. portions were cultured aerobically, using at least 50 cc. of meat-infusion dextrose broth for each 1 cc. of alcohol to be cultured. A 2 per cent. alcoholic solu-

tion is not bacteriostatic and all kinds of spore-bearers were grown with ease in media of this alcoholic content. All cultures were incubated aerobically for two weeks at 37° C. and then for another two weeks at 20° to 22° C. Of the 125 samples, 10 of the absolute alcohol and 50 of the 95 per cent. alcohol samples which were cultured as above were also inoculated and incubated under anaerobic conditions. After one month incubation, none of the 125 samples revealed growth in the above medium when cultured in portions of 1 and 2 cc.

The following experiment revealed that spore-bearing bacteria could survive in 95 per cent. alcohol for varying periods of time. One-tenth cubic centimeter of a one-week broth culture of *B. subtilis* was added to each 30 cc. of 95 per cent. alcohol placed in six-ounce cork-stoppered bottles. A broth culture of *B. megatherium* was added in the same proportion to another bottle containing alcohol. Two six-ounce sets were made, using two different strains of each organism, one in each instance as a check. The containers were stored at room temperature. At intervals of three to four days, 1-cc. and 2-cc. portions of the alcohol containing the added cultures were inoculated into meat-infusion dextrose broth, using at least 50 cc. of medium for each 1 cc. of alcohol cultured. The *B. megatherium* was found to survive in the 95 per cent. alcohol for a period of eighty-eight and ninety-six days respectively, while 215 and 276 days respectively were required for the destruction of the two strains of *B. subtilis*.

Summary

One hundred and twenty-five samples of commercial ethyl alcohol, consisting of 100 samples of 95 per cent. alcohol and twenty-five samples of absolute alcohol, were obtained on the open market from as many different sources as possible. All of these, samples of ethyl alcohol produced in this country, were found to be free of bacteria and their spores. This is in contrast to reports from Europe where the commercial product was found to be contaminated frequently with spore-formers.

Alcohol (95%) did not kill *B. megatherium* and *B. subtilis* until after approximately three months' exposure in the first instance, and seven and nine months respectively were required for the destruction of the two strains of *B. subtilis* used in this experiment.

REFERENCES

- (1) Baker, W. Y.: *Med. Ann., Dist. Col.*, 6, 9, 1937.
- (2) Condamin, F., and Arnulf, G.: *Am. J. Cancer*, 20, 455, 1934 (Abstr.).
- (3) Coulthard, C. E., and Sykes, G.: *Pharm. J.*, 137, 79, 1936.
- (4) Davis, A. A.: *Lancet*, 1, 80, 1936.
- (5) Dogliotti, A. M.: *Rev. Neurol.*, 2, 485, 1931.
- (6) Dozier, C. C.: *J. Infect. Dis.*, 35, 156, 1924.
- (7) Eschenbrenner, H.: *Apoth. Ztschr.*, 102, 1578, 1932.
- (8) Gilcreest, E. L., and Mullen, T. F.: *Surg. Clin. North America*, 11, 989, 1931.
- (9) Heim, L.: *Lehrbuch der Bakteriologie*, Stuttgart, Enke, 1922.
- (10) Knorr, M.: *München. med. Wchnschr.*, 79, 792, 1932.
- (11) Koch, R.: *Mitt. a. d. kais. Gesundh.*, 1, 263, 1881.
- (12) Kuhn, P., and Dombrowsky, K. H.: *München. med. Wchnschr.*, 79, 791, 1932.
- (13) Kurschner, F.: *Pharm. Zentralh.*, 76, 427, 1935.
- (14) Meynier, M. J., Jr.: *Am. J. Obst. and Gynec.*, 32, 265, 1936.
- (15) Minervini, R.: *Ztschr. f. Hyg. u. Infect.*, 29, 127, 1898.
- (16) Newman, H. W.: *Am. J. Psychiat.*, 91, 1343, 1935.
- (17) Nye, R. N., and Mallory, T. B.: *Boston Med. and Surg. J.*, 189, 561, 1923.
- (18) Olitsky, P. K., Traum, J., and Schoening, H. W.: Report of the Foot and Mouth Disease Commission of the United States, U. S. Dept. Agric. Tech. Bull., No. 76, 1928.
- (19) Pozzi, A., and Belleli, D.: *Policlinico (sez. med.)*, 43, 279, 1936 (Abstr., *J. Am. Med. Assn.*, 107, 545, 1936).
- (20) Russ, V.: *Centralbl. f. Bakteriol.*, 37, 280, 1904.
- (21) Ruth, H. S.: *J. Am. Med. Assn.*, 102, 419, 1934.
- (22) Saltzstein, H. C.: *Ibid.*, 103, 242, 1934.
- (23) Schmidt, A.: *Med. Welt.*, 6, 34, 1932.
- (24) Stokvis, C. S.: *Centralbl. f. Bakteriol.*, 48, 440, 1909.

Pumpkin Seeds as an Anthelmintic. F. W. Freise. *Pharm. Zentralhalle* 79, 97 (1938). A large number of wild-growing and cultured pumpkins were examined as to the anthelmintic effect of their seeds. The so-called medullary pumpkin with light-yellow fruits 25-50 cm. long and 12-18 cm. thick and the so-called Italian pumpkin were the most convenient sources for the supply of medicinal seeds. The skin of the germ contains the anthelmintic constituent and seeds which are first dried and then peeled and which contain the germs in a disintegrated condition are useless as anthelmintics. The active constituent represents an alkaloid which is contained in the germs in a concentration of 0.12-0.285 per cent. It has not as yet been isolated in crystalline condition. It is readily soluble in hot water, alcohol and chloroform. A 1-4000 solution kills up to 90 per cent. of added ascarides and oxyurids in five minutes.

L. F. T.

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Bacteriology	Louis Gershenfeld, B. Sc., Ph M.
Biochemistry, Nutrition, etc.	Arno Viehoever, Ph. D.
Biology	Marin S. Dunn, Ph. D.
Chemistry	Arthur Osol, Ph. D.
Pharmacy	E. Fullerton Cook, Ph. M. and their assistants

TRANSMISSION OF DRUGS THROUGH BREASTMILK*

(The following contribution was submitted by Prof. Dr. L. van Itallie of the University of Leiden to supplement an already published abstract on this subject.—Ed.)

IN the January number of this JOURNAL (p. 44) I found an abstract of the *Journ. Pediatrics* 824 (1937) on drugs transmitted through breastmilk. In my laboratory researches on the same subject have been done by Dr. Th. A. G. Haanappel of which some conclusions will be mentioned here.

Iodine—After administration of 1 gm. of sodium iodide the iodine soon appears in the milk (always within 3 hours). The maximum-quantity recovered in 100 cc. milk varied from 2-4 mg. sodium iodide. After three days only traces of iodine could be found in the milk.

Bromine—Bromine is a constant content of human milk, 0.15-0, 25 mg. in 100 cc. milk.

After the administration of 1.3 gm. sodium bromide (= 1 gm. Br) the bromine content of the milk very rapidly increased. The quantities vary from 1-3 mg. in 100 cc. milk.

After administration of 6.5 gm. of sodium bromide, 8 mg. Br were found in 100 cc. milk. After three days the amount was still 3 mg. Br/100 cc. milk.

*Leiden, Pharmaceutical Laboratory of the University.

Arsenic—After administration of 10 mg. arsenic trioxide within twenty-four hours the maximum quantity recovered from 100 cc. milk was 0.01 mg.

This quantity did not increase after administration of 35 mg. within four days.

Quinine—After the administration of 250 mg. of quinine sulfate, not more than 0.1 mg. were found in 100 cc. milk. Twelve hours after the administration the quinine could not more be traced in the milk.

Salicylic acid and Acetylsalicylic acid—After administration of 1 gm. sodium salicylate the quantities recovered from 100 cc. milk varied from 0.4-0.8 mg. After thirty-six hours salicylic acid could not be retraced in the milk.

After administration of 500 mg. acetylsalicylic acid 0.1-0.2 mg. salicylic acid were found in 100 cc. milk. Twelve hours after the administration no more salicylic acid could be retraced.

Claims for Vitamin Products as Recognized by the N. N. R.
J. A. M. A. 110, 577 (1938). Vitamin A may be claimed as a specific for cure of night-blindness due to vitamin A deficiency but not for prevention of colds, influenza, renal calculi or to stimulate growth. Vitamin B may be cited as of value in correcting and preventing beri-beri and certain cases of anorexia of dietary origin and in securing optimal growth of infants and children. It is too early to permit advertising claims for the value of vitamin B₁, in neuritis, intestinal disorders, hyperthyroidism or infections. Vitamin C may be claimed as a corrective measure for scurvy due to a demonstrable absence or suboptimal amount in the diet or in cases in which it is definitely known that there is interference with absorption of an optimal amount. Advertising of vitamin C for such symptoms as failure to gain in weight, stoppage of growth, anorexia, anemia, infections, central nervous disorders or hemorrhagic conditions cannot be accepted unless it is definitely stated that the symptoms are referable to a demonstrable deficiency of vitamin C. Vitamin D is recognized as a specific in the treatment of infantile rickets, spasmophilia, and osteomalacia. There is no warrant for the claims that adequate vitamin D intake will insure normal tooth structure and prevent caries, or that

vitamin D has all the beneficial effects of exposure to sunshine. The Council on Pharmacy and Chemistry still feels convinced that for the present there seems to be no more logical basis for including a variety of vitamins in one preparation than there is for combining a number of other well known dietary essentials in a single pharmaceutical preparation. The Council will, however, accept products containing vitamins A and D together.

L. F. T.

A Slowly Absorbed Epinephrin Preparation (Preliminary Report). Edmund L. Keeney. *Bull. Johns Hopkins Hosp.*, 62 (3): 227, (1938). Purified olive oil was sterilized and placed in sterile vials. Powdered epinephrin base, 2 mg./cc., was weighed and added to the vials under as sterile conditions as possible. After twenty-four hours the suspensions settled out but the particles were readily resuspended by shaking. Supersonic radiation appears to increase the stability of the suspensions, although these suspensions had no greater clinical effectiveness than unirradiated preparations.

Preliminary tests were made on patients, suffering from chronic asthma, who used epinephrine hydrochloride. These tests indicate that the new compound has a more prolonged effectiveness. For example, a morning and evening injection kept three patients free from symptoms for twenty-four hours, while in doses of 1 cc. to 2 cc., they were kept free 8-16 hours. Previously, 5-10 injections of the epinephrin hydrochloride over twenty-four hours were necessary to keep the patients entirely free from asthma.

Additional tests on patients suffering from acute attacks of asthma showed similar longer acting effectiveness.

More recently, suspensions of epinephrin base are being made in peanut oil since it is generally considered, although without experimental evidence, that peanut oil is less irritating than olive oil.

I. C.

Changes in the Official and Tentative Methods of Analysis made at the Fifty-third Annual Meeting of the Association of Official Agricultural Chemists, November, 1937. Compiled by Marian E. Lapp. *Jour. Assoc. Official Agricultural Chemists* 21, 76-98 (1938).

Action of the Association with respect to official and proposed methods of analysis is reported under the various titles recognized in *Methods of Analysis*. The following were adopted as tentative methods of analysis of the drugs listed.

Microchemical Methods: Tests for the identification of apomorphine, benzylmorphine (Peronine), ethylmorphine (Dionine) and hydrastinine with various alkaloidal reagents are given. Methods for the detection of acetylsalicylic acid, benzoic acid and salicylic acid are also described.

Free Iodine in Iodine Ointment: A weighed sample of the ointment is melted in an iodine flask, dissolved in chloroform and titrated with standardized potassium arsenite solution in the presence of potassium bicarbonate, starch being used as the indicator.

Pyridium: Solution of the pyridium in the sample to be tested (tablet, jelly, solution) in hydrochloric acid, or successive extraction with immiscible solvents and hydrochloric acid in the case of ointments, is followed by titration of the active material with standard titanous chloride solution in an atmosphere of carbon dioxide. Light green SF yellowish solution is used as indicator. A blank determination on the reagents and indicator is also performed.

Cinchophen in Presence of Salicylates: The sample is treated with sodium carbonate solution, filtered, the filtrate evaporated to dryness, acidified with glacial acetic acid and mixed with a measured excess of standard iodine solution. After filtration, the excess of iodine is determined by titrating an aliquot portion with sodium thiosulfate solution.

Homatropine in Tablets: A sample of powdered tablets is dissolved in water, alkalinized with ammonium hydroxide and the homatropine extracted with chloroform. After washing with water, the chloroform solution is filtered and evaporated to a small volume on a steam bath, an excess of fiftieth-normal sulfuric acid added and the remainder of the chloroform evaporated. The excess of acid is determined by titration with fiftieth-normal sodium hydroxide in the presence of methyl red as indicator.

Effervescent Potassium Bromide with Caffeine: Potassium bromide is determined in one sample by the Volhard method. In another sample the caffeine is determined by extraction with chloroform, evaporation of the solvent on a water bath and drying to constant weight at 80° C.

Proteolytic Activity of Papain: The prepared enzyme solution, representing 10 milligrams of the original preparation per cc., is mixed with sodium caseinate solution, the whole adjusted to a pH of 5.0 ± 0.1 and incubated for 20 minutes at 40° C. The mixture is then titrated with tenth-normal alcoholic potassium hydroxide in the presence of thymolphthalein indicator, boiling alcohol is added and the titration continued to a persisting pale blue color. A control titration is made as above except that the mixture is not incubated. The unit of papain is defined as that quantity of enzyme which produces a titration difference of 1 cc. of tenth-normal potassium hydroxide and the value of the original preparation is then expressed in units per milligram or as milligrams of the papain preparation necessary to make one unit. Quantities of enzymes giving titration differences of 0.6 to 1.2 cc. of tenth-normal potassium hydroxide are recommended to be used in the analysis. A. O.

Tobacco Smoking and Longevity. R. Pearl. *Science* 87, 216 (1938). A comprehensive study comprising a group of 6,813 males is reported. The cases selected were such as to be as heterogeneous and random as possible except as to the degree of habitual usage of tobacco. In this manner there was obtained a dispersed and counterbalancing effect within each group of all such factors as economic and social status, occupational and racial differences, etc.

Three groupings were compared one containing 2,094 cases who were non-users, a second of 2,814 who were moderate smokers, and a third consisting of 1,905 who were heavy smokers.

Complete life tables were constructed for the three groups starting at age thirty and continuing to the end of the life span by yearly intervals.

The results were quite clear-cut in that the smoking of tobacco was statistically associated with an impairment of life duration and the amount or degree of this impairment increased as the habitual amount of smoking increased. In this study as in many similar mortality studies the difference between usage groups in specific mortality rates practically disappeared from about age seventy on. This is presumably an effect of the residual effect of the heavily selective character of the mortality in the earlier years in the groups dam-

aged by the agent (in this case tobacco). On this view those individuals in the damaged groups who survive to seventy or thereabouts are such tough and resistant specimens that thereafter tobacco does them no further measurable harm as a group. L. F. T.

Common Skin Diseases in Children. E. B. Tauber and George E. Clarke. *Archives of Pediatrics* 15, 1 (1938). A few of the salient facts to be considered in the treatment of the skin conditions most frequently encountered by the pediatrician are stated to be: 1. The sensitivity of the skin of the infant; 2. The unusually rapid response to external stimuli. Due to these conditions the drugs used in the treatment must be chosen with utmost care and caution.

Diaper rash: lesions formed in the diaper region, usually caused by wet or soiled diapers. May become vesicular or papular and may ulcerate if not properly treated. Suggested treatment: Absolute cleanliness of the baby's skin and linen, thorough cleansing of the parts with soap and water, application of an antiseptic and mildly astringent baby powder before placing clean diaper. In the vesicular and papular types the recommended procedure is the same cleansing as before followed by applying a boric acid ointment of 2 to 5 per cent. strength. For the ulcerative stage a solution of Burow's solution 1:64 applied for half hour periods followed by an application of a 2 to 3 per cent. ammoniated mercury ointment is suggested.

In *Impetigo contagiosa* the lesions, if not properly and adequately cared for, may spread to other parts of the body and to other members of the family. Each lesion should be cleansed with soap and water until the crusts have been removed and each eroded surface then coated with a 2 to 5 per cent. ammoniated mercury ointment. Care should be exercised that the infectious material does not contaminate new areas. The fixing of dressings with adhesive plaster is not recommended due to the danger of infection at the point of contact of the plaster and the skin. Isolation, the use of separate soap, face cloths, towels and linen is recommended.

Intertrigo or chafing caused in areas of the skin which lie in apposition, between which perspiration is excessive or retained, may cause superficial ulcerations. The recommended treatment consists of gentle washing with a mild soap and water, careful drying with

a soft linen towel or soft tissue and the application of a soothing dusting powder of fine texture such as zinc stearate, bismuth, starch, acetanilid, chalk, zinc oxide or lycopodium. For the antipruritic effect camphor, menthol or phenol may be added.

Scabies or itch: An infectious disease caused by the burrowing of the impregnated female *acarus scabiei* into the skin, causes intense itching which increases at night. This condition may involve the entire body if treatment is not given. Suggested treatment: the application of sulfur in a 5 per cent. ointment after first bathing in warm soapy water. This treatment is suggested for three successive days after which a hot soapy bath is given and the bed linen changed. In some cases a dermatitis develops from the sulfur, for which colloid baths and the application of a bland ointment—such as boric acid ointment—is suggested.

In eczema which may be either an acute or chronic inflammatory condition, the cause of which is unknown, the suggested treatment is both internal and external. The internal treatment consists of the regulation of the diet, keeping the gastro-intestinal tract open by using mild laxatives and large amounts of water and the administration of tonics, such as cod liver oil and iron compounds to return the physical condition to normalcy.

The external treatment must be selected to fit the type of skin condition of the individual patient. In general, water and particularly soap is detrimental in eczema. Scales and crusts may be removed by non-irritating oils or ointments. The use of Burow's solution, calamine lotion, boric acid and zinc oxide ointments is suggested. For chronic conditions, more stimulating or keratolytic agents such as Lassar's paste with salicylic acid or tar ointment may be used. To allay severe itching the inclusion of menthol or phenol in ointments or lotions is suggested. Many cases of eczema may be relieved by using a colloid bath made by placing one cup of bran or uncooked oatmeal and one tablespoonful of starch in a cloth sack and agitating this in the warm bath water, both before and during bathing.

H. P. F.

Banana Therapy in the Diarrheal Diseases of Infants and Children. C. Loring Joslin, J. Edmund Bradley and Thomas A. Christensen. *Journal of Pediatrics*, 12, 1 (1938). Following the

reports of cases of diarrheal diseases which had responded to banana therapy, the authors conducted a study of sixty-five cases; twenty-two of these were non-specific diarrheas, twenty-one were bacillary dysenteries, both under hospital control and twenty-two were cases of non-specific diarrheas from the out-patient department. The patients were placed on a routine treatment in which banana either as the ripe fruit or as a dehydrated powder was introduced into the diet along with either skimmed milk or buttermilk. Daily records were kept of the weight of the patient and the number and character of the stools.

Charts showing the length of duration of the diarrheas before and after treatment, the number of stools a day before and after treatment and the gain or loss in weight are included in the article.

For infants the dehydrated powder in amounts up to three and one-half tablespoonfuls was given while for older children the fresh, fully ripened fruit in amounts up to nine tablespoonfuls was found to be most satisfactory.

As a result of the treatment and study it was found that 75 per cent. of the cases treated in the hospital gained weight during the attack, the average gain in weight being six ounces, 25 per cent. showed a weight loss and did not gain until the diarrhea subsided. In thirty-six cases of bacillary dysentery treated—fifteen of which were reported in 1935—one death resulted.

From these results the authors concluded banana therapy appears to have helped maintain body weight in diarrheal diseases in infants and children and to have favorably influenced the course of the disease.

H. P. F.

The Use of Helium in Anesthesia. V. H. Eversole. *J. A. M. A.* 110, 878 (1938). A review of the properties of helium is made which led to the use of this inert gas in anesthesia. Barach (*Proc. Soc. Exper. Biol. & Med.*, 32, 462 (1934)) first reported its use in the treatment of patients in status asthmaticus who were completely refractory to epinephrine.

Since helium is entirely inert the basis for its clinical use depends entirely on its physical properties of low specific gravity and rapid rate of diffusion. Helium is approximately one-eighth as heavy as oxygen and one-seventh as heavy as nitrogen, while a mixture of

79 per cent. helium and 21 per cent. oxygen is about one-third as heavy as air and slightly less than one-third as heavy as pure oxygen. Hence on the basis of the formula that $F = MA$, where F is force, M is mass and A acceleration, the force required to move a given volume of 21 per cent. oxygen and 79 per cent. helium should be approximately one-third that required to move the same volume of air. The rate of flow of gases through narrow orifices is inversely proportional to the square root of their molecular weights. On this basis the rate of flow of a mixture of 79 per cent. helium and 21 per cent. oxygen through a narrow orifice should be about twice that of air. Therefore the addition of helium to any gas or mixture of gases will result in a lighter and more diffusible mixture which will require less force (therefore less muscular effort) to be moved. Reasoning from another angle, the same force will move a larger volume of the mixture in a given length of time.

These peculiar physical properties of helium led Barach to employ helium as already mentioned. The present author reports upon the use of helium in certain types of respiratory difficulties during the course of anesthesia such as stridor or obstruction. Although not a substitute for clear and unobstructed breathing it was considered as of distinct value in helping in an emergency until a tube could be inserted into the trachea. It was also considered helpful on many occasions since it permitted the operator to continue the administration of an anesthetic both smoothly and safely without inserting an intratracheal tube when otherwise it would have been necessary.

L. F. T.

Calcium Mandelate. G. Melton and M. L. Rosenheim. *Lancet* 224, 5974 (1938). The use of mandelic acid as a urinary antiseptic has met with two objections: the sodium salt is unpleasant to the taste, causing nausea, and it is necessary to simultaneously administer an acidifying drug such as ammonium chloride. Ammonium mandelate which overcomes the latter objection is both unpleasant to the taste and nauseating. Schnöhr has published some satisfactory results of cases treated with calcium mandelate. Hryntschak has also advocated the use of the calcium compound. Pure calcium mandelate is an insoluble, tasteless, white powder, immiscible with water. It can be given mixed with food or milk or as a

powder and washed down with water. The product used in the cases treated by the authors was prepared by British drug firms.

As reported by other workers when calcium chloride is administered by mouth most of the calcium is excreted in the feces and most of the chloride is absorbed. The action of calcium mandelate is thought to be similar but the mandelic ion—a non-threshold substance—is not retained but is rapidly excreted, the resultant urine besides having a lowered pH contains free mandelic acid. The dosage of calcium mandelate is the same as of all mandelic acid preparations, the equivalent of 3 gm. of mandelic acid four times a day after meals. Clinical results show that calcium mandelate is an effective urinary acidifying agent in both normal persons and those having urinary infections. In a series of thirty-two cases it was necessary to administer additional ammonium chloride in only four cases and in two cases the renal functioning was probably impaired. In a series of thirty-three cases treated, only eight were reported as failures.

Although the author does not believe calcium mandelate to be more effective than the ammonium compound, it is considered to be more pleasant to take and appears to cause less gastric disturbance. The nausea which occasionally occurs lasts generally a day or two and can be avoided by giving the drug at different times with relation to meals. Where renal failure exists the calcium preparation is no more suitable than other mandelic acid preparations.

H. P. F.

The Treatment of Infected Wounds With Urea. Leon F. Muldavin and Jean M. Holtzmann. *Lancet* 224, 5975 (1938). Due to its protein solvent properties, the fact that it is obtainable in quantity and is both cheap and stable, urea was used in the casualty department of the Royal Free Hospital to test its efficiency in the treatment of infected wounds. Wilson (1907) experimenting with urea *in vitro* showed urea solutions of 8 to 25 per cent. retarded bacterial growth and that stronger solutions were bactericidal.

Since no toxic effects were reported from using urea in solid form both saturated solutions and crystals of the compound were used in the experiments. Wounds were syringed free from pus and necrotic material with a saturated solution of urea, excessive mois-

ture removed and the crystals of urea liberally applied. Waxed paper was then applied next to the crystals.

Zinc cream was generally applied to the adjacent area as a protective. During a six months period the cases treated may be classified as, abscesses, infected traumatic wounds of various kinds, infected haematomas, cellulitis, septic wounds due to burns, varicose ulcers, carbuncles and an infected tenosynovitis of the hand. From the detailed notes on seventy of the 170 cases treated with urea the following facts were obtained. A very definite response was generally obtained after two or three applications, sloughs and any foul odor present disappeared. There was no evidence of urea stimulating epithelization. Many wounds healed completely with the urea treatment; in those which did not heal completely the treatment was stopped and a solution to stimulate epithelization was used. No cases developed a urea dermatitis or any evidence of toxic effects. There was no evidence of spreading of sepsis under the urea treatment. In general no pain accompanied the treatment or at the most no pain greater than that in similar cases dressed with other solutions was experienced. All membranes being permeable to urea, no osmotic effect was produced. By dissolving the necrotic material a clean wound was produced which allowed healing to proceed. Even the deepest wounds could be treated by the syringing with the saturated solution.

H. P. F.

Antiplasmodial Action and Chemical Constitution. Part I. Cinchona alkaloidal derivatives and allied substances. A. Cohen and H. King. Part II. Some simple synthetic analogues of quinine and cinchonine by A. D. Ainley and H. King. *Proc. Roy. Soc. Lond., Series B.* 838, Vol. 125, 3, pp. 49, 60 (1938).

PART I.

Experimental bird malaria is utilized for following the effect of changes of structure in the cinchona alkaloids on the therapeutic activity. It is shown that although antiplasmodial action is not very sensitive to stereochemical changes, it is sensitive to changes of structure. Thus there is an apparent loss of activity when the central—CHOH—group is modified in any way. Thus its conversion into—CHCl—, —CH₂— or —CH= leads in almost all cases to an in-

crease in toxicity and loss of antiplasmodial action. The preparation and properties of a series of allied substances is also described.

Authors' Summary.

PART II.

Quinicine (quinotoxine), the ketonic isomeride of quinine, is inactive in bird malaria. Reduction to dihydroquinicinol (2 diastereoisomerides) with reformation of a carbinal group does not restore activity; neither is activity found in α -N-methyldihydroquinicinol. Consideration of these results led the authors to the synthesis of 4-quinolyl- α -piperidylcarbinol, and 4-(6-methoxyquinolyl)- α -piperidylcarbinol, and their N-methyl, N-propyl, N-allyl, N-butyl and N-crotyl derivatives. The only compounds obtained showing antiplasmodial activity were 4-(6-methoxyquinolyl)- α -piperidylcarbinol and its diastereoisomeride *iso*-4-(6-methoxyquinolyl)- α -piperidylcarbinol. These two substances appear to be the first simple substances built on the pattern of the cinchona alkaloid molecule to show antiplasmodial action.

Author's Summary.

I. C.

The Irritative Therapy of Schizophrenia. (1) *American Journal of Psychiatry* 94; 355-372, Sept. 1937; (2) *New York State Journal of Medicine* 37; 1813-1821, Nov. 1937. By Emerick Friedman, M. D., M. S., New York. The technic of the camphor-metrazol-irritative therapy, being a modification of the original procedure developed by v. Meduna, may be described as the deliberate induction of a toxic deliriform or organically confused state punctuated by convulsions, brought on by administering the medullary stimulants, camphor and metrazol, in rather large doses. The patient is first placed on an alkalinizing and hydrating regime for about a week. Camphor-in-oil, 25 per cent. solution, is administered intramuscularly twice daily for one to three weeks, beginning with 16.0 cc. and reaching the maximum dose of 56.0 cc. by increments of 4.0 cc. per day. If convulsions occur at any given dose the injections are omitted the following day, resuming again with the convulsant dose. Intravenous Metrazol injections are started after a lapse of about a day or two with an initial dose of 5.0 cc. of the 10 per cent. solution. The

injections are given on alternate days; as long as a violent grand mal reaction results, the dose is not increased, but if a petit mal or a mild convulsive reaction ensues the subsequent dose is increased by 1.0 cc. A course of treatment is considered as twenty to thirty grand mal reactions depending on the individual case. Camphor produces an increasingly intense, deliriform psychomotor activation with infrequent but at times repeated convulsions; all of which take place usually in the space of three hours after the injection. Metrazol brings on an immediate, typical epileptic form convulsion—grand or petit mal—associated with anxiety, terror, and considerable responses on the part of the whole autonomic nervous system. After about ten convulsive reactions there is noted a fragmentation of the sensorium and apathy which persists until two weeks after the last injection. Out of forty cases of schizophrenia of varying types and chronicities treated by irritative therapy, thirty-one cases displayed definitely remissive changes, which in all but three cases has persisted from about three months to one year. Four were somewhat improved and five were unaffected by the treatment. The only complications were: two cases of dislocated jaws, two of subcutaneous abscesses, two severe tongue lacerations. The theoretical *modus operandi* of the irritative regime may be set forth as follows: (1) Biological antagonism between schizophrenia and the convulsive state (Meduna). (2) Chemical union, metabolism, and elimination of cell-bound toxic agents. (3) Prolonged irritation of the central nervous system as noted by psychomotor upheavals and deliriform states may change the functional barriers to integrated thought-volitional-motor activities. (4) Severely activated internal vertiginous activity as well as decerebrate activity superseded by phenomena of neuro-physiological reintegration. (5) Summoning of responses of the entire vegetative nervous system to meet the threat of disorganization set in action by medullary irritation.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

Professor Kasner defines a *googol* as 10 to the hundredth power (10^{100}), and a *googolplex* as 10 to a power represented by a *googol* (10 to the *googol* power). This latter number is so great that we could go out to the farthest star and then make a tour of the nebulae, writing down zeros all the way in an attempt to express it. Professor Kasner thinks that a suspended book might move upwards towards the hand holding it within a *googolplex* of years, or within some other larger finite number of years.

We suspect that this erudite coiner of a new arithmetical term simply purloined the man-in-the-street's *googoo*, a slangster's word for "queer" or "balmy". And speaking of *googols*, consider for a moment these dimensions.

Molecules vary in size from 0.2 of a millimicron to 5×10^{-8} , or 0.000000005 meters.

The diameter of an electron is 3.8×10^{-15} meters.

The diameter of the nucleus of the hydrogen atom is 2×10^{-18} meters.

The diameter of the nucleus of the gold atom is 4×10^{-17} meters.

A human red corpuscle is 8×10^{-6} meters in diameter.

The smallest visible particle is 5×10^{-5} meters in diameter.

When we consider that, according to the calculations by Einstein, the universe in which we live is 11,731,392,000,000,000,000 miles in diameter, we can gain some general idea of the vast number of unit particles of matter which compose it.

Googols again!

The Pittsburgh Press champions the cause of a boy chemist, a real prodigy who has a grievance against the local pharmacies. States the Press:

"Martin Sokol, five, chemist and student of Shakespeare, gave the neighborhood druggists a piece of his mind—quite a mind, too—last night because they won't sell him the stuff he needs to make gunpowder in his laboratory.

"The boy prodigy charged that the druggists had entered into a conspiracy in restraint of trade and had agreed not to sell him salt-peter on the theory that he was too young to go into the munitions business. Martin also suspects that he is on the blacklist for sulfuric acid and phosphorus."

As usual the druggist is "durned if he does and durned if he don't."

Although the world knows him primarily as the man who invented the sulfur-mining process, Herman Frasch, a former Philadelphia druggist, was a highly successful engineer, chemist and inventor before he became interested in sulfur. He was born in Germany in 1852, but came to the United States when he was only sixteen years old to continue his work as a pharmacist. For a while he worked with Professor John M. Maisch, of this College, and Director of the United States Army Laboratory during the Civil War, but later bought his own drug store in Philadelphia.

Frasch paid very little attention to the actual operation of his drug store—he let his assistant run the store while he spent his time in the laboratory in the back of the store just "fiddling around" as he himself described it. However, his "fiddling" was not at all trivial because in a few years, when he was only twenty-four years old, he was granted his first patent—a process for refining paraffin wax. The oil companies then in operation had been attempting unsuccessfully, to refine paraffin wax for some time, and when Frasch's patent was announced they immediately became interested in both the man and his process. The result was that he sold his drug store to his assistant and went to work for the Standard Oil Company, ultimately becoming one of America's outstanding inventors in this field.

Many of the old-fashioned herbs that are used in seasoning dishes can be grown right in the kitchen window in flower boxes.

The Department of Agriculture, at Washington, which makes this suggestion, says the best herbs to grow in a window are mint, watercress, parsley, rose geranium, chives, sweet marjoram, and basil. The best soil for them is one-part sharp sand, one part well-rotted cow manure, two or three parts of good garden loam, and a little bone meal, all well mixed together.

Last year the sea mining plant at Wilmington, N. C., actually claimed from old Atlantic's waters all the bromine in a square mile of water, 229 feet deep, and found the business so profitable that it paid no attention to the following potential wealth of other chemicals dumped back into the ocean:

Sodium chloride or kitchen salt, 2,140,000 tons, worth \$33,200,000.

Epsom salts, 542,500 tons, worth \$18,050,000.

Calcium chloride, 118,000 tons, worth \$2,570,000.

Potassium chloride, 61,000 tons, worth \$4,880,000.

Magnesium, 48,000 tons, worth \$33,600,000.

Aluminum, 139 tons, worth \$58,200.

Strontium carbonate, 160 tons, worth \$99,600.

Iron, 145 tons, worth \$17,300.

Copper, 9.2 tons, worth \$2,760.

Three tons of iodine, valued at \$10,300.

Enough gold to make a five-inch cube valued at \$42,000.

Silver worth \$29,300—enough to make a ball twenty-five inches in diameter.

The municipal street cleaning department of Stuttgart, Germany, has decided, after several years of experimenting, to operate its several hundred trucks with sewage gas. At present the department is operating one large garbage truck and two small vehicles with sewage gas and the remainder of the fleet is now being converted, according to a report from the American consulate at Stuttgart. Philadelphia sends its sewage down the Delaware, with its compliments to Chester and Wilmington, and its garbage is a monopoly of favored politicians, when it might be turned to city profits.

Said Thomas Huxley—and so well:

“That man, I think, has had a liberal education who has been so trained in youth that his body is the ready servant of his will, and does with ease and pleasure all the work that, as a mechanism, it is capable of; whose intellect is a clear, cold, logic engine, with all its parts of equal strength, and in smooth working order; ready like a steam engine to be turned to any kind of work, and spin the gossamers as well as forge the anchors of the mind; whose mind is stored with a knowledge of the great and fundamental truths of nature and of the laws of her operations; one who, no stunted ascetic, is full of life and fire, but whose passions are trained to come to heel by a vigorous will, the servant of a tender conscience; who has learned to love all beauty, whether of nature or of art, to hate all vileness, and to respect others as himself.”

On July 1st, 1785, William Withering, a doctor of medicine, sat in his little brown house on Market Square in Birmingham, England, and wrote for the preface of his little book “An account of the foxglove, and some of its medical uses, etc.,” the following paragraph:

“The use of the Foxglove is getting abroad, and it is better the world should derive some instruction, however imperfect, from my experience, than that the lives of men should be hazarded by its unguarded exhibition, or that a medicine of so much efficacy should be condemned and rejected as dangerous and unmanageable.”

This was the Doctor Withering who, taking his cue from the old Welsh woman of Shropshire, told the medical world at large the therapeutic worth of digitalis.

From a sere, brown book, the work of this modest, but searching worker of the fallow early days of medicine, we reproduce a quaint case record, with the still quainter, encouraging comment “and on the 6th day of May was discharged perfectly cured,” which in a clin-

ical report is the equivalent of the fairy story end "they lived happily ever afterward."

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HOSPITAL CASES.
C A S E CLXI.

1784.

Mary Hollis, aged 62, was admitted an out patient of the Birmingham General Hospital February 12th, 1784, labouring under all the effects of hydrothorax; her dread of suffocation during sleep was so great, that she always reposed in an elbow chair. She was directed to take two grains of *Digitalis* in powder every night and morning, and for a few days found great relief; but, on the eighth day, as she had complained of sickness, and had been considerably purged, she was ordered to desist taking any more of her powders. On the 14th day she was ordered an ounce of the following infusion twice in a day: *R. Fol. Digital. purp. ficc. ʒiiss. aq. bullient. lbjs. digere per femihoram, colaturæ adde tinct. aromatic ʒi.* This infusion did not purge, but sometimes excited nausea, though not sufficient to prevent her from continuing its use. She grew gradually better, and on the 6th of May was discharged perfectly cured. The diuretic effects of the *Digitalis* were in this instance immediate.

The origin of the so-called Philadelphia scrapple is interestingly recorded by the late Dr. Charles H. LaWall, as follows: Wheat flour was rather scarce during the Revolutionary days, corn more plentiful. Mush was boiled almost every afternoon for the mush and milk supper. That left over was fried for breakfast and served with molasses. A Dutch housewife of New Holland, Lancaster County, was making hog's head cheese, on a butchering day—and by some mistake used too much water. When the meat was tender it was seasoned with sage, garlic, salt and pepper; it was too thin to form a cheese. So—she skimmed out the meat, put it to mold, using as much liquor as would jelly nicely.

"Now what will I do with this liquor; it will not make a good soup—and it must not be wasted."

A neighbor helper suggested making it into a mush to fry. This was done and called Scrap-all and to this day in certain parts of Pennsylvania it is served with molasses. The Germans called it Pon-horse.

Refrigeration by ice or snow was known in very early times. Even Solomon refers to it in Proverbs xxv-13 where he says: "As the cold of snow in the time of harvest so is a faithful messenger to them that send him, for he refresheth the soul of his masters."

Broccoli is not a new vegetable as some seem to believe. It was known to the Romans and was a very popular vegetable in 17th Century France. All cook books of a century or more ago make mention of it and give directions for its preparation. Turnips were highly esteemed as a vegetable by the Romans of the time of Pliny, who states that some single specimens weighed as much as forty pounds. To which we might add "wass you dere Pliny?"